

Application No.: 10/664,513  
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### AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

#### Claims:

1. (Currently amended) A method for assessing metabolic fitness or aerobic demand of a living system, comprising:
  - a) administering an isotopically labeled precursor molecule to the living system for a period of time sufficient for the a label of said isotopically labeled precursor molecule to be incorporated into a mitochondrial molecule in said living system;
  - b) measuring the an isotopic content, isotopic pattern, rate of change of isotopic content, or rate of change of isotopic pattern of said mitochondrial molecule; and
  - c) calculating the a rate of synthesis or degradation of said mitochondrial molecule to assess metabolic fitness or aerobic demand of said living system.
2. (Original) The method of claim 1, wherein the isotopically labeled precursor molecule is labeled with a stable isotope.
3. (Original) The method of claim 1, wherein the isotopically labeled precursor is selected from the group consisting of  $^2\text{H}$ -labeled glucose,  $^{13}\text{C}$ -labeled glucose, a  $^2\text{H}$ -labeled amino acid, a  $^{15}\text{N}$ -labeled amino acid, a  $^{13}\text{C}$ -labeled amino acid,  $^2\text{H}$ -labeled acetate,  $^{13}\text{C}$ -labeled acetate, a  $^2\text{H}$ -labeled ribonucleoside, a  $^{13}\text{C}$ -labeled ribonucleoside, a  $^{15}\text{N}$ -labeled ribonucleoside, a  $^2\text{H}$ -labeled deoxyribonucleoside, a  $^{13}\text{C}$ -labeled deoxyribonucleoside, a  $^{15}\text{N}$ -labeled deoxyribonucleoside, a  $^2\text{H}$ -labeled fatty acid, and a  $^{13}\text{C}$ -labeled fatty acid.
4. (Original) The method of claim 1, wherein the isotopically labeled precursor molecule is  $^2\text{H}_2\text{O}$ .

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5. (Original) The method of claim 1 wherein the isotopically labeled precursor molecule is  $^{13}\text{C}$ -glycine.
6. (Original) The method of claim 1, wherein the label of said isotopically labeled precursor is a radioactive isotope.
7. (Currently amended) The method of claim 1, wherein the isotopically labeled precursor molecule is selected from the group consisting of  $^3\text{H}$ -labeled glucose,  $^{14}\text{C}$ -labeled glucose, a  $^3\text{H}$ -labeled amino acid, a  $^{14}\text{C}$ -labeled amino acid,  $^3\text{H}$ -labeled acetate,  $^{14}\text{C}$ -labeled acetate, a  $^3\text{H}$ -labeled ribonucleoside, a  $^{14}\text{C}$ -labeled ribonucleoside, a  $^3\text{H}$ -labeled deoxyribonucleoside, a  $^{14}\text{C}$ -labeled deoxyribonucleoside, a  $^3\text{H}$ -labeled fatty acid, and a  $^{14}\text{C}$ -labeled fatty acid.
8. (Original) The method of claim 1, wherein the mitochondrial molecule is a deoxyribonucleic acid (DNA).
9. (Original) The method of claim 1, wherein the mitochondrial molecule is a ribonucleic acid (RNA).
10. (Original) The method of claim 9, wherein the RNA is selected from the group consisting of ribosomal RNA, transfer RNA, and messenger RNA.
11. (Original) The method of claim 10, wherein the RNA is messenger RNA.
12. (Original) The method of claim 1, wherein the mitochondrial molecule is a protein.
13. (Original) The method of claim 12, wherein the protein is selected from the group consisting of a subunit of cytochrome c oxidase, a subunit of  $\text{F}_0$  ATPase, a subunit of  $\text{F}_1$  ATPase, a subunit of cytochrome c reductase, and a subunit of NADH-CoQ reductase.
14. (Original) The method of claim 1, wherein the mitochondrial molecule is a lipid.

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15. (Original) The method of claim 14, wherein the lipid is a phospholipid.
16. (Original) The method of claim 15, wherein the phospholipid is selected from the group consisting of cardiolipin, phosphatidylcholine, phosphatidylethanolamine, and a mixture thereof.
17. (Original) The method of claim 1, wherein the living system is a tissue.
18. (Original) The method of claim 17, wherein the tissue is muscle.
19. (Original) The method of claim 18, wherein the muscle is skeletal muscle or cardiac muscle.
20. (Original) The method of claim 17, wherein the tissue is adipose tissue.
21. (Currently amended) The method of claim 1, wherein ~~the step of said~~ measuring isotopic content, pattern or rate of change of isotopic content, or pattern is performed by mass spectroscopy spectrometry, NMR spectroscopy, or liquid scintillation counting.
22. (Original) The method of claim 1 wherein the isotopically labeled precursor molecule is administered orally.
23. (Original) The method of claim 1, wherein the living system is an animal.
24. (Original) The method of claim 23, wherein the animal is a mammal.
25. (Original) The method of claim 24, wherein the mammal is a rodent.
26. (Original) The method of claim 24, wherein the mammal is a human.
27. (Original) The method of claim 1, wherein the living system is a cell.

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28. (Original) The method of claim 27, wherein the cell is a platelet.
29. (Original) The method of claim 27, wherein the cell is a cultured cell in a high-throughput screening assay system.
30. (Original) A method of identifying a drug agent capable of altering metabolic fitness or aerobic demand of a living system comprising:
- a) assessing the metabolic fitness or aerobic demand of the living system according to claim 1;
  - b) administering the drug agent to said living system; and
  - c) assessing the metabolic fitness or aerobic demand of the living system according to claim 1, wherein a change in the metabolic fitness or aerobic demand of the living system before and after administration of the drug agent identifies the drug agent as capable of altering the metabolic fitness or aerobic demand of the living system.
31. (Original) The method of claim 30, wherein the living system is a mammal.
32. (Original) The method of claim 31, wherein the mammal is a human.
33. (Original) The method of claim 31, wherein the mammal is a rodent.
34. (Original) The method of claim 30, wherein the living system is a cell.
35. (Original) The method of claim 34, wherein the cell is a cultured cell in a high-throughput screening assay system.
36. (Original) The method of claim 35, wherein the isotopically labeled precursor molecule is contacted with cell culture media.

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37. (Original) The method of claim 30, wherein the drug agent is tested for the ability to prevent deconditioning of a living system.
38. (Original) The method of claim 30, wherein the drug agent is tested for the ability to increase metabolic fitness or aerobic demand in response to an exercise or other training regimen.
39. (Original) A method of identifying a drug agent capable of altering metabolic fitness or aerobic demand of a living system comprising:
- a) assessing the metabolic fitness or aerobic demand of a first said living system according to claim 1, wherein the drug agent has not been administered to said first living system;
  - b) assessing the metabolic fitness or aerobic demand of a second said living system according to claim 1, wherein the drug agent has been administered to said second living system;
  - c) comparing the metabolic fitness or aerobic demand in said first and second living systems, wherein a change in the metabolic fitness or aerobic demand of the first and second living systems identifies the drug agent as capable of altering the metabolic fitness or aerobic demand of the living system.
40. (Original) The method of claim 39, wherein the living system is a mammal.
41. (Original) The method of claim 40, wherein the mammal is a human.
42. (Original) The method of claim 40, wherein the mammal is a rodent.
43. (Original) The method of claim 39, wherein the living system is a cell.
44. (Original) The method of claim 43, wherein the cell is a cultured cell in a high-throughput screening assay system.

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45. (Original) The method of claim 44, wherein the isotopically labeled precursor molecule is contacted with cell culture media.
46. (Original) The method of claim 39, wherein the drug agent is tested for the ability to prevent deconditioning of a living system.
47. (Original) The method of claim 39, wherein the drug agent is tested for the ability to increase metabolic fitness or aerobic demand in response to an exercise or other training regimen.
48. (Original) A kit for assessing the metabolic fitness of a living system, comprising:
- a) one or more isotopically labeled precursor molecules; and
  - b) instructions for use of the kit,
- wherein the kit is used to measure metabolic fitness.
49. (Original) The kit of claim 48, further comprising a tool for administering the isotopically labeled precursor molecule.
50. (Original) The kit of claim 48, further comprising an instrument for obtaining a sample from the subject.
51. (Original) The kit of claim 48, wherein said isotopically labeled precursor molecule is isotopically labeled water.
52. (Original) A drug agent identified by the method of claim 30.
53. (Original) A drug agent identified by the method of claim 39.
54. (Original) An isolated isotopically perturbed mitochondrial DNA.

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- 55. (Original) An isolated isotopically perturbed cardiolipin.
- 56. (Original) One or more isolated isotopically perturbed mitochondrion.
- 57. (Original) An isotope-labeled precursor molecule.
- 58. (Original) An isolated isotope-labeled mitochondrial molecule made by administering an isotope-labeled precursor molecule to said host organism for a period of time sufficient for an isotope label of said isotope-labeled precursor molecule to become incorporated into a mitochondrial molecule.